II. REMARKS

Claims 1-33 were pending and were variously rejected under 35 U.S.C. §§ 112, second paragraph, 102 and 103. Applicants acknowledge with appreciation that the subject matter of claim 2 was allowable.

The specification has been amended herein to correct typographical errors in various descriptions of the Figures. The original claims have been canceled and new claims 34-60 have been added in a sincere effort to advance prosecution. Support for the new claims is detailed in the Table below.

Claim	**Support**
34, 35	paragraphs [0010] and [0011] of the specification
36	paragraph [0012] of the specification
37	paragraph [0026] of the specification
38	claim 10 in PCT priority document PCT/US99/30265
39	claim 22 in PCT priority document PCT/US99/30265
40	paragraph [0013] of the specification
41	paragraph [00135] of the specification
42, 43, 51, 52, 58, 59	paragraph [0009] of the specification
44, 53	paragraph [0072] of the specification
47, 54	paragraph [00160] of the specification
46, 55	claim 20 in PCT priority document PCT/US99/30265
47, 56	paragraph [0076] of the specification
48, 59	paragraphs [0016] and [0017] of the specification
50	paragraph [00132] of the specification
57	paragraph [0015] of the specification
60	paragraph [0010] of the specification

No new matter has been added as a result of these amendments and entry thereof is respectfully requested.

In view of the foregoing amendments and following remarks, Applicants respectfully requested reconsideration of the application.

35 U.S.C. 112, Second Paragraph

Previous claim 10 was rejected as allegedly indefinite. In view of the foregoing amendments canceling claim 10, Applicants submit that this rejection has been obviated.

35 U.S.C. § 102

Previous claims 1, 3, 5, 7, 10, 11, 13, 15, 23 and 24 were rejected as allegedly anticipated under 35 U.S.C. § 102(b) by U.S. Patent No. 5,320,102 (hereinafter "Paul"). In support of these rejections, it is alleged that Paul teaches "a method of treating a human with a joint disorder involving cartilage as claimed by applicant including obtaining an electronic MRI image of the joint having both normal and diseased cartilage tissue, electronically evaluating the image to obtain information of volume, thickness and other characteristics, and selecting a therapy based on the information." (Office Action, page 2).

Applicants traverse the rejections and supporting remarks.

In order to be an anticipatory reference, the single reference cited by the Office must disclose each and every element of the claims. *Hybritech v. Monoclonal Antibodies,* 231 USPQ 81 (Fed. Cir. 1986). Moreover, the single source must disclose all of the claimed elements arranged as in the claims. *See, e.g., Richardson v. Suzuki Motor Co.,* 9 USPQ2d 1913 (Fed. Cir. 1989).

Paul fails to disclose each and every element of the previous claims. Similarly, Paul fails to teach or suggest the elements of the pending claims. Paul is directed entirely toward diagnosing proteoglycan deficiency in cartilage by quantifying pixel intensity of a two-dimensional MRI. In contrast, any pending claims related to biochemical mapping specify that a three-dimensional map of the cartilage is made. Thus, Paul fails to disclose or suggest the claimed methods. Accordingly, Applicants request that the rejection be withdrawn.

35 U.S.C. § 103(a)

Previous claims 4, 6, 12, 14 and 25 stand rejected as allegedly obvious over Paul in view of U.S. Patent No. 6,205,411 (hereinafter "DiGioia"). In addition, claims 8, 9, 16-22 and 26-33 stand rejected as allegedly obvious over Paul in view of U.S. Patent No. 6,316,153 (hereinafter "Goodman"). Paul is cited as above. DiGioia is cited for allegedly teaching a method of therapy for diseased tissue including the step of osteochondral grafting. (Office Action, page 3).

Goodman is cited for allegedly teaching three-dimensional mapping of tissue for tissue engineering. The Office then asserts that it would have been obvious to combine Paul with DiGioia or Goodman to arrive at the invention of claims 4, 6, 8, 9, 12, 14, 16-22, 25 and 26-33. (Office Action, page 3).

Applicants traverse the rejection and supporting remarks.

The Office bears the burden of establishing a *prima facie* case of obviousness. *See, e.g., In re Ryckaert,* 28 USPQ2d 1955, 1956 (Fed. Cir. 1993); and *In re Oetiker,* 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). In order to establish a *prima facie* case of obviousness, the cited references must teach or suggest all the limitations of the claims. *See, In re Wilson,* 165 USPQ 494, 496 (CCPA 1970). The Federal Circuit has repeatedly held that using "hindsight reconstruction" to provide the necessary motivation is improper. (see, e.g., *In re Fine,* 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) and *In re Napier* 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) stating that "obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention absent some teaching, suggestion or incentive supporting the combination."). Further, common knowledge and common sense are not the specialized knowledge and expertise necessary to establish a motivation to arrive at the claimed invention. See, *e.g., In re Lee,* 61 USPQ2d 1430 (Fed. Cir. 2002).

The combination of references cited by the Office does not teach or suggest all the elements of the previous or pending claims. In addition, there is no motivation in any of the references to arrive at the claimed methods or to combine them as suggested by the Examiner. As noted above, the claimed methods are directed to methods of assessing cartilage over time or to methods of providing a three-dimensional biochemically-based map of cartilage. For the reasons detailed above, Paul is entirely limited to diagnosis of proteoglycan deficiency in cartilage in two-dimensions. Thus, there is no motivation in Paul to arrive at the claimed invention.

The secondary references do not in any way supply what is missing from Paul. DiGioia is directed to methods of inserting an implant. At best, this reference discloses evaluating the skeletal geometry -- an entirely different pursuit than evaluating cartilage geometry. Like DiGioia, Goodman is entirely silent as to cartilage and, moreover, this reference is specifically limited to creating small physical models, where small is defined as less than 1 micron. (See, *e.g.,* Abstract). Thus, neither of the secondary references teaches the elements of the pending

claims that are missing from the primary references and neither provide the motivation to arrive at the claimed invention (or suggest its desirability). Accordingly, the obviousness rejection is improper and Applicants respectfully request that it be withdrawn.

III. CONCLUSION

In view of the foregoing remarks, Applicants submit that the pending claims are sufficiently definite and define an invention that is described, enabled and patentable over the art of record. Accordingly, Applicants submit that the claims are now in condition for allowance and request early notification to that effect.

Should the Examiner have any further questions, Applicants request that the undersigned be contacted at (650) 325-7812.

Respectfully submitted,
Cooley Godward LLP

Date: 17 Jan 03

By: D Pasternak
Dahna S. Pasternak
Registration No. 41,411
Attorney for Applicants

COOLEY GODWARD LLP
Five Palo Alto Square
3000 El Camino Real
Palo Alto, CA 94306
Telephone: (650) 843-5608
Facsimile: (650) 857-0663

Version Showing Changes Made to Specification)

Paragraph [0040] is amended as follows:

--Figures 8A and 8B show a 3-point Dixon GRE image of the articular cartilage of medial femorotibial compartment in a normal 35-year old volunteer. Figure ~~13A~~ 8A has the subject in a supine position and Figure ~~13B~~ 8B has the subject in an upright position.--

Paragraph [0042] is amended as follows:

--Figure ~~9B~~ 11B is a 2D cartilage thickness map demonstrating abrupt decrease in cartilage thickness in an area of the defect (arrows). The) thickness between the neighboring pixels can be [use] used to define the borders of the cartilage defect. Note defused cartilage thinning in the area enclosed by the asterisks (*).--

Paragraph [0043] is amended as follows:

--Figures 10A-10C show a 3D surface registration of femoral condyles based on T1-weighted Spin-Echo MR images. Figure ~~6A~~ 10A is baseline with a knee [and] in neutral position. Figure ~~6B~~ 10B is a follow-up with knee and external rotation with a 3D view that is the identical to the one used in ~~6A~~ 10A but the difference in knee rotation is apparent. In Figure ~~6C~~ 10C, transformation and re-registration of Scan Bin to the object coordinate system of Scan A shows the anatomic match to A is excellent.--

Currently Pending Claim Set

34. (New) A method of assessing the change of cartilage in a joint of a mammal over time, the method comprising the steps of

(a) determining the thickness, width, area or volume of a region of cartilage at an initial time T_1;

(b) determining the thickness, width, area or volume of the region of cartilage at a later time T_2; and

(c) determining the change in the thickness, width, area or volume of the region of cartilage between the initial and the later times.

35. (New) The method of claim 34, wherein the steps (a) and (b) comprise obtaining a three-dimensional map of the region of cartilage.

36. (New) The method of claim 34, further comprising the steps of:

electronically transferring an electronically-generated image comprising the cartilage from a transferring device to a receiving device located distant from the transferring device;

receiving the transferred image at the distant location; and

converting the transferred image to a degeneration pattern.

37. (New) The method of claim 36, wherein the joint is from a human and wherein the method further comprises the step of generating a movement pattern for the joint of the human from a database accessible to the distant location, wherein the database includes a collection of movement patterns of human joints, which patterns are organized and are accessed by reference to characteristics such as type of joint, gender, age, height, weight, bone size, type of movement, and distance of movement.

38. (New) The method of claim 37, wherein the movement pattern is of a human walking, running, stair-climbing, stepping onto/off of a platform, or jumping.

39. (New) The method of claim 37, wherein the movement pattern and the electronically-generated image are merged to show how the movement pattern interacts with the electronically-generated image.

40. (New) The method of claim 34, wherein the volume of the cartilage loss is assessed by determining the thickness, D_N, of the normal cartilage near the cartilage defect;

obtaining the thickness of the cartilage defect, D_D, of the region;

subtracting $_{DD}$ from D_N to give the thickness of the cartilage loss, D_L;

determining the area of the cartilage defect A_D; and

multiplying the D_L value times the area of the cartilage defect, A_D, to give the volume of cartilage loss.

41. (New) The method of claim 40, wherein the region of the cartilage defect includes a portion of the cartilage contiguous to the defect.

42. (New) The method of claim 34, wherein the joint is a knee joint.

43. (New) The method of claim 34, wherein the mammal is a human.

44. (New) The method of claim 34, wherein the thickness, width, area or volume of the region of cartilage is obtained from a magnetic resonance imaging (MRI) technique.

45. (New) The method of claim 44, wherein the MRI technique includes placing external markers on the skin overlaying the bone on either side of the joint.

46. (New) The method of claim 44, wherein the MRI technique first obtains a series of two-dimensional views of the joint, which are then mathematically integrated to give a three-dimensional image.

47. (New) The method of claim 44, wherein the MRI technique employs a gradient echo, spin echo, fast-spin echo, driven equilibrium fournier transform, spoiled gradient echo or steady state free precession technique.

48. (New) A method of making a three-dimensional map of joint cartilage of a mammal, wherein the joint comprises cartilage and associated bones on either side of the joint, which method comprises

(a) measuring a detectable biochemical component;

(b) determining the relative amounts of the biochemical component; and

(c) mapping the amounts of the biochemical component in three dimensions, thereby making a three-dimensional map of joint cartilage.

49. (New) The method of claim 48, further comprising the step of determining the areas of abnormal joint cartilage by identifying the areas having altered amounts of the biochemical component present.

50. (New) The method of claim 48, wherein the biochemical component are glycosaminoglycan, sodium, water or hyaluronic acid.

51. (New) The method of claim 48, wherein the joint is a knee joint.

52. (New) The method of claim 51, wherein the mammal is a human.

53. (New) The method of claim 50, wherein measuring of the biochemical component is done using a magnetic resonance imaging (MRI) technique.

54. (New) The method of claim 53, wherein the MRI technique includes placing external markers on the skin overlaying the bone on either side of the joint.

55. (New) The method of claim 53, wherein the MRI technique first obtains a series of two-dimensional views of the joint, which are then mathematically integrated to give a three-dimensional image.

56. (New) The method of claim 55, wherein the MRI technique employs a gradient echo, spin echo, fast-spin echo, driven equilibrium Fourier transform, spoiled gradient echo or steady state free precession technique.

57. (New) A method of estimating the change of cartilage in a joint, wherein the joint comprises articular cartilage, the method comprising the steps of

(a) defining a 3D object coordinate system of the joint at an initial time, T_1;

(b) identifying a region of a cartilage defect or diseased cartilage within the 3D object coordinate system;

(c) defining a volume of interest around the region of the cartilage defect or diseased cartilage whereby the volume of interest is equal to or larger than the region of cartilage defect or diseased cartilage, but does not encompass the entire articular cartilage;

(d) defining the 3D object coordinate system of the joint at a second timepoint, T_2;

(e) placing the identically-sized volume of interest into the 3D object coordinate system at timepoint T_2 using the object coordinates of the volume of interest at timepoint T_1; and

(f) measuring any differences in cartilage within the volume of interest between timepoints T_1 and T_2.

58. (New) The method of claim 57, wherein the joint is a knee joint.

59. (New) The method of claim 57, wherein the mammal is a human.

60. (New) The method of claim 57, wherein measuring the differences shows a loss of the cartilage between T_1 and T_2.